REMARKS

Claims 1-13, 25-28, and 30-41 are pending.

The amendment to claim 4 is supported by Examples 1-9 in the specification. Applicants submit that the amendment to claim 4 would not narrow the scope of the amended recitation because it would have been apparent to a person skilled in the art that "the amino acid sequence of SEQ ID NO:2" in claim 4 as filed refers to the amino acid sequence inside the thermostable DNA polymerase according to claim 4. The amendments to claims 5, 32 and 35-38 are merely cosmetic. The amendment to claim 5 merely delete redundant claim recitations. The amendment to claim 32 should not narrow the scope of the amended claim recitation because, it would have been apparent to one skilled in the art that, "a-like DNA polymerase" is a typographical error for "α-like DNA polymerase." The amendment to claim 35 merely deletes "said" before "the" to correct redundancy. The amendments to claims 36-38 merely insert "the" for cosmetic improvement. It would have been apparent that "histidine (H)" in claims 36-38 refers to H in the $DX_1EX_2X_3X_4H$ sequence recited in claim 1.

The new claims 39-41 are supported by the specification at page 21, lines 4-11, page 22, line 13 to page 23, line 5, and page 23, lines 14-19.

Election by Original Presentation

Applicants respectfully disagree that claim 31 is patentably distinct from the invention of claims 11-13, 25-28, 30 and 32-38 because "the product can be made by a materially different process such as chemical synthesis" as alleged by the Office Action. Claim 31 is drawn to a method of improving amplification efficiency and/or fidelity of a thermostable DNA polymerase. Applicants query how chemical synthesis can improve the amplification and /or fidelity if the main thing involved is an enzyme, i.e. a thermostable DNA polymerase. Applicants request that claim 31 be rejoined with the other examined claims because applicants submit that the allegation of "the product can be made by a materially different process such as chemical

synthesis" is not supported by scientific reasoning. If the election by original presentation is to be maintained, applicants request that the Patent Office describes what chemical synthesis would improve the amplification efficiency and/or fidelity of a thermostable DNA polymerase.

Claim Rejections - 35 U.S.C. 112

(A) Indefiniteness Rejection

Applicants respectfully traverse the indefiniteness rejection of claims 25-28 and 30. The Office Action does not put forth any reason why claims 25-28 and 30 were deemed to be indefinite. Claims 25-28 and 30 used to be rejected as indefinite in the previous Office Action of December 27, 2002 because claims 25-28 and 30 depended on claim 1, which was rejected by the previous Office Action as indefinite. Now claim 1 is no longer rejected as indefinite, the indefiniteness rejection of claims 25-28 and 30 should be withdrawn.

Concerning the indefiniteness rejection of claims 4-12 and 32, applicants also respectfully traverse the rejection. The rejection is rendered moot because of the amendment to claims 4, 5 and 32. The modified thermostable DNA polymerase of claim 4 comprises an amino acid sequence of SEQ ID NO:2 with replacement of the histidine residue at location 147 (see DIETLYH) with another amino acid. Thus, the indefiniteness rejection of claims 4-12 should be withdrawn.

Applicants also request that the indefiniteness rejection of claim 32 be withdrawn because of the replacement of "a-like DNA polymerase" with "α-like DNA polymerase."

Written Description Rejection

Applicants respectfully traverse the written description requirement of claims 1-12, 25-28, 30 and 32-38. Applicants submit that the claimed invention was adequately described to a person skilled in the art in the specification and claims 1-30 as filed. For instance, the subject matter of these claims are described the specification at pages 5-13 and 20-24, as well as

Examples 1-9.

In particular, regarding the written description rejection of claims 1-3, 25-28, 30 and 32-38, the specification provides sufficient written description because the specification describes a modified thermostable DNA polymerase comprising a $DX_1EX_2X_3X_4H$ sequence within the exonuclease I region of the thermostable DNA polymerase, wherein histidine(H) has been replaced by another amino acid, as now claimed, wherein the modified thermostable DNA polymerase has modified 3'-5' exonuclease activity and/or amplification efficiency.

In making the rejection, the Office Action states that "there is no disclosure of any particular structure to function/activity relationship in the disclosed species." Applicants respectfully disagree. Page 20, line 19 to page 24, line 3 of the specification describes the effects of replacing histidine in the $DX_1EX_2X_3X_4H$ sequence with acidic, neutral or basic amino acids. For instance, replacement of H in the $DX_1EX_2X_3X_4H$ sequence with an acidic amino acid results in a thermostable DNA polymerase with reduced 3'-5' exonuclease activity and improved amplifying efficiency (e.g. page 20, line 19 to page 21, line 3, and page 21, lines 23 to page 22, line 4, of the specification). Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with a neutral amino acid results in a thermostable DNA polymerase with improved amplifying efficiency (e.g. page 21, lines 4-12, page 22, line 13 to page 23, line 5; and page 23, lines 14-19, the specification). Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with a basic amino acid results in a thermostable DNA polymerase with improved 3'-5' exonuclease activity and/or fidelity in DNA replication (e.g. page 21, lines 13-22, the specification). See also Figures 2-4. Thus, there is disclosure of the particular structure to function/activity relationship in the modified thermostable DNA polymerase according to the claims.

Withdrawal of the indefiniteness rejection is requested.

(B) Non-Enablement Rejection

Applicants respectfully traverse the non-enablement rejection of claims 1-12, 25-28 and 30. Applicants disagree with the Office Action's allegations that the art is unpredictable and

"there is no disclosure of any particular structure to function/activity relationship in the disclosed species." Page 20, line 19 to page 24, line 3 of the specification discloses the particular structure to function/activity relationship in various species of the modified thermostable DNA polymerase according to the claims. Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with an acidic amino acid results in a thermostable DNA polymerase with reduced 3'-5' exonuclease activity and improved amplifying efficiency (e.g. page 20, line 19 to page 21, line 3, and page 21, lines 23 to page 22, line 4, of the specification). Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with a neutral amino acid results in a thermostable DNA polymerase with improved amplifying efficiency (e.g. page 21, lines 4-12, page 22, line 13 to page 23, line 5, and page 23, lines 14-19, the specification). Replacement of H in the $DX_1EX_2X_3X_4H$ sequence with a basic amino acid results in a thermostable DNA polymerase with improved 3'-5' exonuclease activity and/or fidelity in DNA replication (e.g. page 21, lines 13-22, the specification). See also Figures 2-4. Thus, there is disclosure of the particular structure to function/activity relationship in the modified thermostable DNA polymerase according to the claims. The disclosure of the particular structure to function/activity relationship in the specification shows that the effects of replacing the histidine residue in the thermostable DNA polymerase are not unpredictable. The scope of the claimed invention is not overly broad in light of the disclosure. The disclosure shows how thermostable DNA polymerases having an exonuclease region I can be modified by replacing histidine in the $DX_1EX_2X_3X_4H$ sequence of the exonuclease region I. The disclosure of the function/activity relationship provides ample guidance to a person skilled in the art how to practice the claimed invention. With the disclosure and the knowledge of the art, a person skilled in the art can practice the claimed invention without undue experimentation. Applicants respectfully disagree with the Office Action's assertion that only the claimed invention involving a thermostable DNA polymerase having SEQ ID NO:2 is enabled. The Office Action does not put forth any credible technical reason or evidence why the Patent Office doubts applicants' disclosure of the operability of the claimed invention. The enabling disclosure is commensurate in scope with the claims. Withdrawal of the non-enablement rejection is requested.

Conclusion

In light of the above reasoning, applicants submit that the application is in a condition for allowance. A Notice of Allowance is believed in order.

In the event that this paper is deemed not timely, applicants petition for an appropriate extension of time. The petition fee, and any other fees that may be required in relation to the filing of this paper, can be charged to Deposit Account No. 11-0600, referencing Docket No. 10089/14.

Respectfully Submitted,
KENYON & KENYON

Date: June 29, 2004

King L. Wong
King L. Wong, Ph.D.
Registration No. 37,500

1500 K Street, NW, Suite 700
Washington, D.C. 20005
202-220-4200 (tel)
202-220-4201 (fax)
DC01 496135v1